Chapter No. II

REVIEW OF LITERATURE

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Chapter II

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2.1 Anatomy and physiology of urinary system

The urinary system consists of a pair of kidneys and ureters, a bladder and a urethra (Plate No. 1 & 2). Various metabolic waste products, such as creatinine, urea and uric acid are eliminated by this system from the body. Kidneys also eliminate xenobiotics such as exogenous drugs and toxins. Kidneys are responsible for maintaining volume and electrolyte balance of body fluids by excreting excess of inorganic substances ingested in the diet. It is also a site of production of hormones renine and erythropoietin, 1,25 dihydroxycholecalciferol, prostaglandins and kinins. Kidney also catabolises small molecular weight proteins and is the site of aminogenesis and gluconeogenesis.

Kidneys form a paired organ system located in the retroperitoneal space and extend from the twelfth thoracic to the third lumbar vertebrae. In adult each kidney is about 12cm long and weight about 150gm in men and 135gms in women. Each kidney has a concave mediate border called the renal hilum, where the kidneys are functionally connected to the body. Anatomically kidneys are divided in two parts i.e. outer cortex and inner medulla. The medullary substance forms pyramid. From the base of each medullary pyramid, parallel arrays of tubules, the medullary rays penetrate the cortex. Each
Plate No. 1: Kidneys and Retroperitoneal cavity (in female)

1. Diaphragm
2. Inferior vena cava
3. Renal artery
4. Kidney (left)
5. Renal vein
6. Ureter
7. Proximal major muscle
8. Common iliac artery and vein
9. Recto-uterine pouch of Douglas
10. Uterus
11. Round ligament of uterus
12. Vessico-uterine pouch
13. Peritoneum (cut)
14. Urinary bladder
15. Abdominal part of esophagus
16. Aorta
17. Superior mesenteric artery
18. Iliac crest
19. Sigmoid colon
20. Uterine tube and ovary
21. Adrenal gland
22. Renal calices
23. Renal pelvis
24. Quadratus lumborum muscle
25. Rectum
26. Dorsal duct
27. Urethra and penis
28. Testis and epididymis
29. Testicular artery and vein
30. Inguinal ligament
31. Lumbar vertebrae
32. Liver
33. Spleen
34. Small intestine
35. Pancreas
Plate No. 2: Ureters

- Abdominal aorta
- Right renal artery
- Left renal artery
- Right kidney
- Left kidney
- First constriction - ureteropelvic junction
- Testicular arteries
- Ureter
- Second constriction - pelvic inlet
- Common iliac artery
- Internal iliac artery
- External iliac artery
- Third constriction - entrance to bladder
- Bladder
medullary ray consists of one or more collecting tubules together with the straight portions of several nephrons (Plate No. 3).

The Renal pelvis :-

The expanded upper end of the ureter (the tube joining the kidney to urinary bladder), which is divided into two or three major calyces from which several small branches, the small calyces arises.

Nephrons :-

Nephrons are the functional unit of kidney. Each kidney contains about 400,000 nephrons each consists of dilated portion, the renal corpuscle, the proximal convoluted tubules, the thin and thick limbs of loop of henle, the distal convoluted tubule and collecting duct.

Glomerulus :-

Glomerulus are formed from a specialized capillary network and surrounded by a double walled epithelial capsule called Bowman’s capsule, which forms the beginning of the proximal convoluted tubules (PCT).

Proximal convoluted tubule (PCT) :-

Proximal convoluted tubule is the most metabolically active part of the nephron. The reabsorption of (60-80%) glomerular filtrate is facilitated by proximal convoluted tubule, where sodium, chloride, potassium, glucose,
Plate No. 3: Internal Structure of the Kidney
phosphate, bicarbonate, sulfate, amino acid, citrate, lactate and acetate reabsorption takes place by PCT. Creatinine is secoreated by PCT and hydrogen is excreted by the kidneys.

**Loop of Henle :-**

Loop of Henle is a 'U' shaped portion of urineferous tubule. It is consisting of Ascending limb of Loop of Henle and Descending limb of Loop of Henle. Thin limb of loop of Henle is having ability to generate concentrate urine which is hypertonic with respect to serum.

**Descending limb of Loop of Henle :-**

The cationic and anionic organic waste products like urate, hippuric acid, oxalic acid, bile salts produces by liver and drugs, are secreted by active transport against a concentration gradient at the basolateral surface of cell followed by passive diffusion across the luminal plasma membrane into tubule fluid in this region.

**Distal Tubules :-**

Distal tubule includes three morphologically distinct segments

i) The thick ascending limb (TAL) of Henle's loop

ii) The macula densa

iii) The distal convoluted tubule.
Sodium chloride (NaCl) actively reabsorbs by the thick ascending limb, which is mediated by \( \text{Na}^+/\text{K}^+/\text{Cl}^- \) co-transport. The calcium and magnesium from the tubular fluid is also absorbed by thick ascending limb. Bicarbonate transport mechanism located on the basolateral plasma membrane of thick ascending limb (TAL).

The distal convoluted tubule is an ion exchange site, which controls the total salts and water in the body and maintains the acid base balance by the secretion of hydrogen and ammonium ions into the tubular urine.

**Collecting duct :-**

The collecting duct represents the final site in the renal tubule that modifies the volume and solute composition of the tubule fluid.

**Uraters :-**

There is a one pair of tube which joins two kidneys with the urinary bladder, called urater.

**Bladder and urinary passages :-**

The urine formed by the kidneys is stored in urinary bladder through ureter. It is then excreted outside through urinary passage.
Urethra :-

The urethra is a tube that carries the urine from the bladder to the exterior. In the female, the urethra is exclusively a urinary organ but in male, seminal fluid also passes through it during ejaculation.

Urine :-

Urine is a fluid produced by kidneys as a result of filtration, reabsorption and elimination processes. It is stored in urinary bladder and when bladder is full it passes through urethra to out of body.(E. Koushanpour and W. Kriz, 1986; L. Carlos Junqueira et al., 1995; Carl A. Burtis et al., 2001).

2.2 Prevalence and incidence :-

The epidemiology of nephrolithiasis remains poorly investigated in the different region. Prevalence and incidence rates are mostly based on hospital admissions. Countries of the region show wide variations in prevalence and site of stone formation. About 50% of patients have a single stone with no recurrence, but the other 50% have recurrent episodes within 5 years. The incidence of the nephrolithiasis is higher in industrialized nations as compared with developing countries.

The stone burden remains high in males (Male: Female, 2:1) with peak ages in the 3rd and 4th decade in most country of the region. In India prevalence rate of nephrolithiasis is 15% and composition of renal stones are as
follows —

i) Calcium oxalate  74%
ii) Uric acid and urate  03%
iii) Struvite  22%
iv) Other  01%

The rate of acute episodes are higher during hot rather than the cold weather (Rizvi S. A. H et al., 2002; Husain M. et al., 1995).

2.3 Diseases of the kidneys and urinary tract:


Syndromes in nephrology:

1] Acute or rapidly progressive renal failure.
3] Chronic renal failure
4] Nephrotic syndrome
6] Urinary tract infection
7] Renal tubule defects
8] Nephrolithiasis.
2.4 Nephrolithiasis :-

Nephrolithiasis is a common condition, where formation of stone in kidney takes place. The stone is designated as renal stone, kidney stone, renal calculi or urinary calculi. Renal calculi are polycrystalline aggregates composed of varying amounts of crystallloid and a small amount of organic matrix (Schaul G. Massary et al., 1989). In the kidney the mineral deposits originate as microscopic particles and develop into stone over a time and hence the condition is called nephrolithiasis or renal stone disease.

2.5 Renal stone formation :-

Renal stone formation is not yet fully understood. Many theories of renal calculi formation has been proposed.

2.5.1 Nucleation theory :-

This theory states that presence of certain crystals or foreign body in urine serves as an initiator for crystal growth in a higher supersaturated urine. The nucleation may be homogenous or heterogeneous nucleation. Sodium hydrogen urate, uric acid and hydroxy-appeptite crystals can serves as heterogeneous nuclei that permit calcium oxalate stone formation in supersaturated urine even at lower super-saturation (Lowrence M. et al., 1998; Coe F. L. et al., 1975).
2.5.2 Stone matrix theory :-

The presence of unusual substance described as matrix substance “A” which is possibly a microprotein that “seeds” the formation of calculi. The organic matrix of serum and urinary proteins, albumin, α₁ & α₂ globulins, gamma-globulins, mucoproteins, glycosaminoglycans provides a framework for deposition of crystals (Boyce W. H. and Garvey F. K., 1956; Ryall R. L. et al., 1991; E. bisunos et al., 1993).

2.5.3 Inhibitor absence theory or Inhibition of crystallization theory :-

In normal urine a number of potent inhibitors of stone formation are present. These inhibitors are magnesium, pyrophosphate, citrate, phosphocitrate, mucoproteins, RNA- glycosaminoglycans and various peptides, certain amino acids, urea and trace metals. Low levels or absence of these inhibitors can contribute to the formation of kidney stone (Alex C. et al., 1980; Robertson W. G. and M. Peacock, 1972).

2.5.4 Blocked lymphatic theory :-

The damage to the renal pelvic lymphatic due to infection or other causes, resulting in incompetent lymphatic drainage valves. Protein and other material cannot be removed properly and stone may be nucleated in a pouch outside the urinary tract. Various investigators have accepted the generalized model of stone formation formed by combining these basic theories (Reginold J. Carr
In 1937 Randall made a masterly review of all the current theories of stone formation. He concluded that there must be a lesion in the renal pelvis to which a calculus could remain anchored during its period of growth. On the basis of this assumption, he investigated kidneys obtained from post mortem bodies with the aid of hand lens and found the lesions of the renal papilla now known as "Randall’s plaque" and postulated that this was the basic cause of renal calculus. On microscopic examination he considered these lesions to be plaques of calcium deposited in the interstitial tissue at the tip of the renal papilla and stated definitely that the deposits were not intratubular. He had observed twenty-eight stones, each of which was adherent to or growing upon a papilla and each of these stones was supported by and attached a primary intra papillary calcium plaque as its initiating lesion (Reginald J. Carr 1954).

2.6 Anatomical sites for stone formation :-

It is generally accepted that renal stones are initially formed in the proximal urinary tract and passes progressively into the calices, renal pelvis and ureter (Plate No. 4, 5, 6, 7 & 8).

2.7 Types and chemical composition of Renal Stone :-

Emil A. Tanagho et al., (1992) reported that renal stones are consists of a matrix of mucoprotein (2.5-3%), which is the core of the calculus. The commonest renal stone are of calcium phosphate with or without calcium oxalate. Approximately 85% of stones are composed of calcium compounds.
Plate No. 4: Ureteropelvic Stone

Plate No. 5: Midureteral Stone

Plate No. 6: Lower Ureteral Stone
Plate No. 7 :- Ureteropelvic Stone

Plate No. 8 :-
Upperureteral Stone
Table No. 1: Chemical composition and percentage prevalence of stones

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Chemical composition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Calcium oxalate / phosphate/ Monohydrate/dihydrate/Appetite</td>
<td>75%</td>
</tr>
<tr>
<td>2.</td>
<td>Magnesium ammonium phosphate Hexahydrate</td>
<td>10-15%</td>
</tr>
<tr>
<td>3.</td>
<td>Uric acid</td>
<td>6%</td>
</tr>
<tr>
<td>4.</td>
<td>Mixed magnesium calcium uric acid</td>
<td>3-10%</td>
</tr>
<tr>
<td>5.</td>
<td>Cystine</td>
<td>1-2%</td>
</tr>
<tr>
<td>6.</td>
<td>Xanthine</td>
<td>Rare</td>
</tr>
<tr>
<td>7.</td>
<td>Adenine</td>
<td>Rare</td>
</tr>
<tr>
<td>8.</td>
<td>Drug induced (Indinir, Triamtrene)</td>
<td>1%</td>
</tr>
</tbody>
</table>

2.7.1 Calcium Stones :-

Calcium stones are composed of oxalate or phosphate or mixture of oxalate and phosphate. These stones are regular or irregular, spherical and almost white. Calcium oxalate is the major component of about 80% of all stones and may be present as the monohydrate, the dihydrate or both. The calcium oxalate stones are generally hard and irregular (Stosimirovic B., 1998; Mates J., 1969; Benner R. J., 1982; Blacklock N. F., 1979) (Plate No. 9).

Calcium is most abundant mineral in the human body. Calcium plays an important role in the skeletal mineralization, blood coagulation, neuromuscular conduction and maintenance of normal muscle tone (Woos Cannon D. C., 1984).
Major dietary sources of calcium are milk and dairy products, soybeans, legumes, dark green leafy vegetables, nuts etc. Calcium is absorbed by active as well as passive transport mainly in the small intestine. The intestinal calcium absorption is influenced by dietary factors. Calcium excretion is increases by lactose and reduces by high intestinal pH, oxalate, phytate, free fatty acid, and phosphate. Vitamin D increases intestinal absorption of calcium and excretion of calcium in urine (Curhan G. C. et al., 1993). The calcium metabolism is regulated by parathyroid hormone, vitamin D and calcitonine (Peter N. Campbell et al., 1988) (Flowchart No. 1).
2.7.1.1 Calcium stones are associated with hypercalcaemia :-

a) Hyperparathyroidism:-

Hypercalcaemia is observed in primary hyperparathyroidism, which results in hypercalciuria. The incidence of stone formation among patients with hyperparathyroidism is related to the hypercalciuria. The degree of hypercalciuria is determined by serum 1,25 (OH)₂ D₃ (Broldus A. E., et al., 1980; Muldowney F. P. et al., 1999).

b) Sarcoidosis and other Granulomatus Diseases and lymphomas :-

Patient with sarcoidosis usually form mixed calcium stones composed of calcium oxalate and calcium phosphate. The hypercalciuria in this patient results from increased bone resorption and increased intestinal calcium absorption. (Benner R. J., 1982)

2.7.1.2 Calcium stone associated with hypercalciuria without hypercalcaemia:-

a) Idiopathic hypercalciuria syndrome :-

Renal hypercalciuria is due to inability of the kidney to conserve calcium, occurs in about 10% of all stone forming patients. The cause of the renal leakage of calcium is unknown. The excretion of calcium via urine results in a low serum calcium level, which causes stimulation of parathyroid

b) **Renal tubular acidosis**: -

Nephrolithiasis occurs only in type I renal tubular acidosis, in which there is defect in renal tubular hydrogen ion secretion (Buckalew V. M. Jr., 1989).

**2.7.1.3 Calcium stones associated with hyperuricosuria with or without hypercalciuria**: -

Hyperuricosuria appears to be a powerful promoter of the formation of calcium oxalate stones. Coe (1977) stated heterogeneous nucleation may occur when uric acid crystals act as a nucleus or seed core for the precipitation of calcium oxalate crystals (Gorver P. K. et al., 1990; Coe. F. L., 1977).

**2.7.1.4 Idiopathic calcium stone**: -

Approximately one fourth of calcium stone formers do not exhibit hypercalciuria, hyperoxaluria, hyperuricosuria, Hypocitraturia or a defect in urinary acidification (Loris Borghi et al., 1996; Marnagella M et al., 1999).
I) Hyperoxaluria:

Hyperoxaluria is one of the risk factors in the pathogenesis of calcium oxalate calculi (R. Kumar et al., 2003).

Oxalic acid is a nonessential end product of metabolism. About 40% of oxalate is formed from Ascorbic acid and 40-50% from Glycine metabolism (James M. Orten, 1990) (Flowchart No. 2).

Dietary ingested oxalate is poorly absorbed (12%) from gastrointestinal tract. Enteric bacteria destroy approximately half of the ingested oxalate and about 25% is excreted unchanged in the faeces. All of the absorbed and the endogenously produced oxalate is filtered by the kidney and excreted unchanged in the urine. Intake of oxalate rich food, or its precursors increases excretion of oxalate. These oxalate rich foodstuff such as rhubarb, spinach, tomatoes, strawberries, chocolate and tea causes temporary oxalate excretion in all individuals, known as secondary hyperoxaluria.

Primary hyperoxaluria arises from rare inherited (autosomal recessive) errors of metabolism, in which errors depends on separate enzyme defects in the metabolism of glycine. Stone formation occurs in childhood, recurrences are common and often damage the kidneys and leads to chronic renal failure (J. S. Garrow & W. PT. James, 1993; Monico C. G. and Milliner D. S., 1997)
Flow chart No. 2: - Endogenous pathway of oxalate production. Numbers indicate site of enzyme deficiency in type I and type II primary hyperoxaluria.
Enteric hyperoxaluria occurs in a number of gastrointestinal disorders and also occur or exaggerated by a diet low in calcium (D. L. Earnest, 1979; Modigliani R. et al., 1978).

II) Hypocitraturia: -

Citrate is a by-product of normal oxidative pathway in the body. Citrate is normally excreted in the urine. Tubular absorption of citrate varies with the mitochondrial pH gradient. Citrate is an important inhibitor of urolithiasis, which forms soluble complexes with calcium and inhibits precipitation of calcium oxalate and phosphate and growth of their crystals (Simmi K. Ratan et al., 2002; P. V. R. K. Rao and Sofiya Bano, 2003) (Figure).

III) Hypomagnesuria: -

Magnesium excreted in urine can form complexes with oxalate and thus reduces saturation. Hypomagnesuria is one of the risk factor of calcium oxalate stone (A. Jakasaki E., 1972; O. Myake et al., 1998, Schmiedl A. and S. Chwille P. O. 1996).

IV) Role of macromolecules: -

Some urinary components with high molecular weight (greater than 10,000 daltons) act as protective inhibitors of the crystallization of calcium salt. The qualitative or quantitative alterations of these molecules such
Plate No. 9 :- Calcium oxalate stone

Plate No. 10 :- Uric acid stone
Flow chart No. 3 :- Formation of uric acid from purine nucleosides
glycosaminoglycans (GAG), hydrophilic colloids, phosphopeptides, acidic peptides or RNA-like substances can promote stone formation (Y. Nakagawa et al., 1985; Nakagawa, Y. et al., 1981, Edyvan K. A. et al., 1987; Bek Jensen H and Tiselius H. G. 1991).

2.7.2 Uric acid stones --

Uric acid stones are softer and shows laminations and central nucleus. Uric acid stones are common in patients with gout and are also seen in the tropics (Plate No. 10).

Uric acid is the major end product of purine metabolism in human. It is formed endogenously by breakdown of ATP, nucleic acid, from dietary nucleic acid and by denovo synthesis. (Flow chart No.3)

At physiological pH uric acid is mostly in ionized state and present in plasma as sodium urate. Uric acid in serum is filtered by the glomeruli and reabsorbed uric acid is secreted by the distal renal tubule, excreted in urine, some uric acid excreted via gut (M. M. Chatterji and Rana Shinde, 2002).

About a quarter of patients with uric acid stones have hyperuricosuria. Patients with an inflammatory disease of the bowel such as ulcerative colitis and those with an ileostomy ordinarily excrete highly concentrated acidic urine and have an increased incidence of uric acid stone formation (Eiml A. Tanagho et al., 1992; Grover P. K. et al., 1990).
2.7.2.1 Uric acid stone associated with:-

a) Metabolic abnormality:-

Patients with a metabolic abnormality such as primary gout or lesh- Nyhan-Syndrome forms uric acid calculi (F. P. Anita, 1989).

b) Calculi associated with chronic dehydration :-

Patient with chronic diarrhea or those with ileostomies are known to be more prone for the formation of uric acid stones. Excessive perspiration, low intake of fluid also decreases urinary volume and leads to stone formation (Eiml A. Tanagho et al., 1992).

c) Calculi associated with Hyperuricosuria without hyperuricemia :-

Drugs such as thiazide diuretics and salicylates can cause hyperuricosuria and leads to uric acid stone formation (Yendt S. R. et al., 1970).

d) Idiopathic uric acid Lithiasis :-

Patients with idiopathic calculi do not have hyperuricemia or hyperuricosuria tend to excrete persistently acidic urine (Eiml A. Tanagho et al., 1992).

2.7.3 Cystine stones :-

The cystine stones are insoluble and shows tree like appearance with irregular surface and shape (Plate No. 11). The cystinuria is
Plate No. 11: Cystin stone

Plate No. 12: Triple Phosphate stone
relatively rare autosomal recessive inborn error of metabolism, characterized by impaired reabsorption of dibasic amino acids such as cystine, lysine, ornithine and arginine. Excessive excretion of cystein leads to crystallization within the renal pelvis and stone formation (Burns J. R. and Harick L. C., 1986). The urine of patients with cystine calculi is often acidic and contains classic hexagonal cystine crystals (Dahlberg, P. J., 1977; Mog T Tanase I. et al., 1994).

2.7.4 Triple phosphate stone :-

These stones are also known as struvite or infective stones. These stones are associated with chronic urinary tract infection occur about two fold in women as compared to men (Donald P. Griffith et al., 1976). These stones are composed of magnesium ammonium phosphate and carbonate appetite (Plate No. 12).

Struvite stones tend to form in urinary tract infections with urea splitting bacteria, such as proteus species pseudomonas, klebsiela and staphylococcus because these organisms forms alkaline urine by increasing concentration of bicarbonate and ammonium ion. Thus the urine becomes super saturated with the components of struvites and stone forms. (Neelam Seth et al., 1997; Nemoy N.J. and Stamey T.A., 1971; Griffith D.P., 1978; Rodman S., 1999).

2.7.5 Xanthine and adenine stone :-

These stones are very rare.
• High doses of vitamin C and vitamin D
• Low intake of vitamin B6.
• High intake of oxalate.

b) **Heredity Factor:**

Detailed family history may show that some of the blood relations of a patient with kidney stones may have similar trouble. There may be hereditary defect of metabolism that predisposes the persons to stone formation.

c) **Climate and fluid intake:**

The persons in hot tropical climates are more prone for development of urinary calculi. In hot tropical climate a lot of fluid is lost through perspiration and hence concentrated urine is formed and more exposure to sunlight causes Vit. D synthesis and thereby increases intestinal calcium absorption.

d) **Chemical Factors:**

• High levels of calcium, cystine, oxalate, uric acid and sodium in the urine.
• A low level of citrate and magnesium in urine.

e) **Pathological Conditions:**

• Colitis
• Gouty Arthritis
2.10 Evaluation of patient with nephrolithiasis:

Evaluation of patient with nephrolithiasis is not only important during the pathogenesis of stone but also after recovery from surgical removal of stone. In general, patients with detectable abnormality in the composition of blood or urine can account for current or further stone formation will require on going therapy to prevent recurrences (Pak C. Y. C. et al., 1980; Better O. S. et al., 1978).

2.11 Signs and Symptoms of kidney stone:

The Small, Smooth Kidney Stones may remain in the kidney or passes without causing pain called as silent stones. The stones that lodge in the ureter cause the urinary system to spasm and produce Pain. The pain is related to the size of the stone and often radiates from the lower backside (Sir Stanely Davidson and John Macleod, 1998).

The larger stones usually does not passes and require medical intervention. There are various symptoms of kidney stones such as-

- Blood in the urine (Hematuria).
- Increase frequency of urination.
• Pain during urination (stinging, burning).
• Tenderness in the abdomen and kidney region.
• Urinary tract infection.
• Nausea and vomiting.

2.12 Laboratory diagnosis of nephrolithiasis :-

The laboratory diagnosis of nephrolithiasis can be done by imaging test and laboratory test (Sir Stanely Davidson and John Macleod, 1998; Charles Y. C. et al., 2002; Pak C. Y. C. 1991).

a. Imaging test :-

Following imaging tests are used to diagnose nephrolithiasis-

• Ultrasound
• Plain abdominal X-Ray.
• Intravenous pyelogram (IVP)
• Retrograde pyelogram.
• Computerized tomography (CT) Scan.

b. Laboratory test :-

Laboratory tests are not only important to reveal the cause but also important for the management and prevention of further episodes of
1. Chemistry Panel
   a. Serum electrolytes
   b. Serum calcium
   c. Serum phosphorus
2. Renal function test
   a. Blood urea / Blood urea nitrogen
   b. Serum creatinine
   c. Serum uric acid
   a. Qualitative analysis of stone
   b. Microscopic crystal analysis
      i. Envelope shape crystal – Calcium oxalate
      ii. Diamond shape crystal – Uric acid
      iii. Coffin lid crystal – Struvite
      iv. Hexagonal – Cystine
5. Urine culture and Sensitivity
Twenty Four Hours urine analysis:

i. Urine calcium
ii. Urine phosphorus
iii. Urine sodium, potassium and chloride
iv. Urine uric acid
v. Urine Creatinine
vi. Urine oxalate
vii. Urine citrate
viii. Urine magnesium

2.13 Crystals in urine:

Crystals are not normally present in freshly passed urine and are precipitated from solution as the urine cools. Generally crystals in the urine are of no significance, except crystals of sulfonamides, cystine, oxalate in persons with a history of urethral colic or stone formation, and possibly, urates in those with gout (Tiselius H. G. et al., 1995; V. H. Talib, 1999).

A. Crystals Appearing in Acidic urine:

i] Calcium oxalate:

These are colorless, octahedral crystals and appear as small
squares crossed by two diagonal lines. In another form calcium oxalate crystals are
dumbbell-shaped. They vary greatly in size, dissolved in mineral acid (Plate
No. 13 bottom).

ii]  Uric acid :-

Uric acid crystals are usually yellow to pink or radish brown in
color. They are rosettes as plates, barrel shaped, occur in acidic urine. These
crystals are dissolved in sodium hydroxide (Plate No. 14).

iii] Urates :-

The urate crystals occur in acidic urine, in the form of mono or
disodium salt of ammonium. They appear as amorphous sediment. The shape
of ammonium urate is spherical and covered with spikes "Thorn Apple". These
crystals are heat soluble.

iv] Cystine :-

These crystals are rarely seen and found in inborn error of
metabolism of cystine termed as cystinuria. These are colorless, hexagonal plates,
soluble in alkali, mineral acid whereas insoluble in water, acetic acid, and ethanol
(Plate No. 15).

v] Leucine and Tyrosin :-
Plate No. 13: Triple Phosphate and Calcium oxlate crystals

Plate No. 14: Uric Acid crystals

Plate No. 15: Cystin crystals
liver disease. Tyrosin crystals are Sheaves or tufts of fine needle shaped, while leucin crystals are spherical shaped. They are soluble in acids and alkalies.

B. **Crystals appearing in alkaline urine** :-

i] **Phosphates** :-

Phosphates often appear as amorphous sediment, soluble in acetic acid (Plate No. 13 - top).

ii] **Ammonium magnesium phosphate (Triple phosphate) :-**

They are colorless, prism with three, four or six sides and oblique surface at the ends feathery, fern like variety. They are soluble in acetic acid.

iii] **Calcium hydrogen phosphate** :-

They are star shaped clusters “Stellar phosphates” irregular colorless plates or flakes.

iv] **Calcium carbonate** :-

Crystals appears as dumbbells, spheres or amorphous granules, soluble in acetic acid.
v] Magnesium phosphate :-

These crystals are rhombic plates.

vi] Ammonium urate :-

These crystals can appear in round, oval or thorn apple form. They are soluble in acids.

C. Other Crystals: -

i] Sulfonamide :-

Crystals appear in the urine after administration of sulpha drugs.

ii] Xanthine :-

These crystals found extremely rare, small colorless rhombic, plates, soluble in water and dilute ammonia.

iii] Cholesterol :-

A cholesterol crystal occurs in diseases of kidney. The shape of crystals is rectangular or rhombic plate with notched corners. These are soluble in ether, ethanol, chloroform but insoluble in water, acid and alkali.
2.14 Urological Treatment of nephrolithiasis:

- Stones having less than 6mm diameter passed spontaneously hence patients does not require surgical intervention and are treated with analgesics and fluids.

- Patient with stones having 6-10mm diameter requires surgical intervention and depends on presence and degree of ureteral striction.

- Patients with stones in lower ureter can be extracted cystoscopically.

- Patients with pelvic and upper ureteral stones require surgical removal or recently by extracorporial shock lithotripsy followed by prophylactic antibiotic administration.

- In some patients extra corporial lithotripsy is not feasible or successful then percutaneous nephrostolithotomy and direct ultrasonic lithotripsy may be used for stone removal or disintegration.

- Patients with large calculi especially struvit staghorn are usually treated by a combination extra corporial and percutaneous lithotripsy (Pak C. Y. C., 1991; Wickhan J. E., 1993).